What is claimed is:

1. Microspheres comprising an active ingredient dispersed within a polymeric composition comprising a first pH insensitive hydrophobic polymer and second pH sensitive hydrophobic polymer, wherein the microspheres, in an aqueous environment having a pH of around 5 or greater, release the active ingredient in a substantially zero-order profile, and wherein:

(a) the microspheres are formed by a non-aqueous emulsion solvent evaporation method in which the first and second polymers and active ingredient are dispersed in an organic solvent to form a polymer solution phase, the polymer solution phase is emulsified into a second continuous phase comprising a second solvent and a surfactant to form an emulsified dispersion system, and the emulsified dispersion system is agitated and organic solvent evaporated therefrom to form the microspheres;

(b) the concentration of the second polymer as a percentage of total polymer in the polymer solution phase ranges from around 1% to 35% and total polymer concentration in the polymer solution phase ranges from around 5% to around 35%;

(c) microsphere particle diameter ranges from approximately 25μm to approximately 1,000μm;

(d) the weight percentage of active ingredient in a microsphere ranges from around 5% to around 50%; and

(e) active ingredient concentration is highest in the microsphere core.

2. Microspheres of claim 1, wherein:

(a) the first and second polymers are selected from the group consisting of cross-linked polyvinyl alcohol, , polyvinyl chlorides, regenerated insoluble non-erodible cellulose, acylated cellulose, esterified celluloses, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate diethyl-aminoacetate, polyurethanes,

polycarbonates, and microporous polymers formed by co-precipitation of a polycation and a polyanion modified insoluble collagen;

(b) the organic solvent is a halogenated hydrocarbon, an alcohol, acetonitrile, or ketone, or mixture thereof;

(c) the second solvent is silicone oil, sesame oil, soybean oil, corn oil, cottonseed oil, coconut oil, linseed oil, mineral oil, n-hexane, n-heptane, or mixtures thereof; and

(d) the surfactant is an anionic surfactant, nonionic surfactant, polyoxyethylene-castor oil derivative, polyvinylpyrrolidone, polyvinyl alcohol, lecithin, or sorbitan sesquioleate, or mixtures thereof.

3. Microspheres of claim 1, wherein the first and second polymers are selected from the group consisting of cellulose acetate dimethylamino acetate, cellulose acetate ethyl and methyl carbonate, cellulose acetate phthalate, cellulose acetate succinate, cellulose acetate chloroacetate, cellulose diacetate, cellulose triacetate, cellulose acetate ethyl oxalate, cellulose acetate trimellitate, hydroxypropyl methylcellulose phthalate, cellulose acetate methyl and butyl sulfonate, cellulose acetate octate, cellulose acetate laurate, cellulose acetate p-toluene sulfonate, cellulose acetate ethyl carbamate, cellulose acetate methyl carbamate, cellulose acetate valerate, cellulose acetate maleate, and combinations and mixtures thereof.

4. Microspheres of claim 1, wherein the first and second polymers are selected from the group consisting of cellulose acetate, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate trimellitate, cellulose propionate butyrate, and combinations and mixtures thereof.

5. Microspheres of claim 1, wherein the first polymer is cellulose acetate butyrate (CAB) and the second polymer is cellulose acetate phthalate (CAP).

6. Microspheres of claim 5, wherein the total concentration of polymer in the polymer solution phase is between around 5% to around 15%.

7. Microspheres of claim 6, wherein the total concentration of CAP in the polymer solution phase as a percentage of total polymer is between around 1% to 30%.

8. Microspheres of claim 7, wherein the average microsphere size is 100 μm to 700 μm.

9. Microspheres of claim 8, wherein the total concentration of CAB in the polymer solution phase is between around 7% to around 9%, the total concentration of CAP in the polymer solution phase as a percentage of total polymer is between around 1% to 3%, and the microspheres are 150 μm to approximately 350 μm in size.

10. Microspheres of claim 8, wherein the microspheres comprise around 30% to around 35% by weight of one or more of the following active ingredients: an alpha-adrenergic agonist an analgesic or anti-migraine agent, an anti-allergic agent, an anesthetic agent, an anoretic agent, a anti-bacterial (antibiotic) agent an anti-cancer agent, an anti-cholinergic agents an anti-diabetic agent, an anti-emetic agent, an anti-fungal agent an antihistamine agent, an anti-hyperlipoproteinemic agent, an anti-hyperthyroid agent , an anti-inflammatory or corticoid agent, an anti-malarial agent, an anti-Parkinson's or Anti-Alzheimer's agent, an anti-psychotic, anti-anxiety or anti-depressant agent, an anti-ulcerative agent, an anti-viral agent, an anxiolytic agent, a B-Adrenergic agonist agent, a bronchodilator, a cardioactive agent, a central nervous system stimulant, a cholinergic agent, a muscle relaxant, and a narcotic antagonist agent.

11. Microspheres of claims 5 or 9, wherein the organic solvent is acetone , the surfactant is sorbitan sesquioleate, and the active ingredient is theophylline.

12. Microspheres of claim 5, wherein, upon dispersion of the microspheres into an aqueous environment having a pH of around 5 or greater, substantially all of the active ingredient is released from the microspheres in between around 12 to 24 hours.

13. Microspheres of claim 12, wherein substantially all of the second polymer dissolves in the aqueous environment upon release of substantially all of the active ingredient from the microspheres.

14. A controlled-release pharmaceutical composition comprising microspheres of claims 1, 5, or 9.

15. A controlled-release pharmaceutical composition of claim 14, wherein the pharmaceutical composition is a tablet.

16. A controlled-release pharmaceutical composition of claim 14, wherein the pharmaceutical composition is administered orally, parenterally, by inhalation spray, topically, rectally, nasally, buccally, vaginally or via an implanted reservoir

17. A controlled-release pharmaceutical composition of claim 14, wherein the pharmaceutical composition is a tablet or capsule which, upon administration to a mammal, releases substantially all of the active ingredient in the mammal's small intestine.

18. Microspheres comprising an active ingredient dispersed within a polymeric composition comprising a first pH insensitive hydrophobic polymer and second water-swellable polymer, wherein the microspheres, in an aqueous environment, release the active ingredient in a substantially zero-order profile, and wherein:

(a) the microspheres are formed by a non-aqueous emulsion solvent evaporation method in which the first and second polymers and active ingredient are dispersed in an organic solvent to form a polymer solution phase, the polymer solution phase is emulsified into a second continuous phase comprising a second solvent and a surfactant to form an emulsified dispersion system, and the emulsified dispersion system is agitated and organic solvent evaporated there from to form the microspheres;

(b) the concentration of the second polymer as a percentage of total polymer in the polymer solution phase ranges from around 0.25% to 10%, total polymer concentration in the polymer solution phase ranges from around 5% to around 35%, and the viscosity of the polymer solution phase ranges from around 20 cps to around 1000 cps, preferably about 50 to about 300 cps;

(c) microsphere particle diameter ranges from approximately 25μm to approximately 1,000μm;

(d) the weight percentage of active ingredient in a microsphere ranges from around 5% to around 50%; and

(e) active ingredient concentration is highest in the microsphere core.

19. Microspheres of claim 18, wherein:

(a) the first polymer is selected from the group consisting of cross-linked polyvinyl alcohol, polyolefins, polyvinyl chlorides, cross-linked gelatins, regenerated insoluble non-erodible cellulose, acylated cellulose, esterified celluloses, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate diethyl-aminoacetate, polyurethanes, polycarbonates, and microporous polymers formed by co-precipitation of a polycation and a polyanion modified insoluble collagen;

(b) the second polymer is selected from the group consisting of a low-substituted cellulose ether or internally cross-linked cellulose derivatives of sodium carboxymethylcellulose, hydroxypropyl-methylcellulose (HPMC), a hydroxypropylcellulose (HPC), a poly(ethylene oxide), an hydroxyethylcellulose, or a hydrogel forming polymer;

(c) the organic solvent is an alcohol, acetonitrile, ketone, or mixture thereof;

(d) the second solvent is silicone oil, sesame oil, soybean oil, corn oil, cottonseed oil, coconut oil, linseed oil, mineral oil, n-hexane, n-heptane, or mixtures thereof; and

(e) the surfactant is an anionic surfactant, nonionic surfactant, polyoxyethylene-castor oil derivative, polyvinylpyrrolidone, polyvinyl alcohol, lecithin, or sorbitan sesquioleate, or mixtures thereof.

20. Microspheres of claim 19, wherein the first polymer is selected from the group consisting of cellulose acetate dimethylamino acetate, cellulose acetate ethyl and methyl carbonate, cellulose acetate succinate, cellulose acetate chloroacetate, cellulose diacetate, cellulose triacetate, cellulose acetate ethyl oxalate, cellulose acetate methyl and butyl sulfonate, cellulose acetate octate, cellulose acetate laurate, cellulose acetate p-toluene sulfonate,

cellulose acetate ethyl and methyl carbomate, cellulose acetate valerate, cellulose acetate maleate, and combinations and mixtures thereof.

21. Microspheres of claim 20, wherein the first polymer is selected from the group consisting of cellulose acetate, cellulose acetate propionate, cellulose acetate butyrate, cellulose propionate butyrate, and combinations and mixtures thereof.

22. Microspheres of claim 20, wherein the second polymer is a hydrogel former.

23. Microspheres of claim 18, wherein the first polymer is cellulose acetate butyrate (CAB) and the second polymer is hydroxypropylcellulose (HPC).

24. Microspheres of claim 23, wherein the total concentration of polymer in the polymer solution phase is between around 5% to around 15%.

25. Microspheres of claim 24, wherein the total concentration of HPC in the polymer solution phase as a percentage of total polymer is between around 0.25% to 10%.

26. Microspheres of claim 25, wherein the average microsphere size is 100 μm to 400 μm.

27. Microspheres of claim 26, wherein the total concentration of CAB in the polymer solution phase is between around 7% to around 9%, the total concentration of HPC in the polymer solution phase as a percentage of total polymer is between around 0.5% to 3%, and the microspheres are 150 μm to approximately 350 μm in size.

28. Microspheres of claim 27, wherein the microspheres comprise up to around 35% by weight of one or more of the following active ingredients: an alpha-adrenergic agonist an analgesic or anti-migraine agent, an anti-allergic agent, an anesthetic agent, an anoretic agent, a anti-bacterial (antibiotic) agent an anti-cancer agent, an anti-cholinergic agents an anti-diabetic agent, an anti-emetic agent, an anti-fungal agent an antihistamine agent, an anti-hyperlipoproteinemic agent, an anti-hyperthyroid agent , an anti-inflammatory or corticoid agent, an anti-malarial agent, an anti-Parkinson's or Anti-Alzheimer's agent, an anti-psychotic, anti-anxiety or anti-depressant agent, an anti-ulcerative agent, an anti-viral agent, an anxiolytic agent, a B-Adrenergic agonist agent, a bronchodilator, a cardioactive agent, a

central nervous system stimulant, a cholinergic agent, a muscle relaxant, and a narcotic antagonist agent.

29. Microspheres of claim 27, wherein the organic solvent is acetone, the surfactant is Arlacel 83, and the active ingredient is theophylline.

30. Microspheres of claim 23, wherein, upon dissolution in an aqueous environment having a pH of around 5 or 6 or greater, substantially all of the active ingredient is released from the microspheres in between around 12 to 24 hours.

31. A controlled-release pharmaceutical composition comprising microspheres of claims 18, 23, or 27.

32. A controlled-release pharmaceutical composition of claim 31, wherein the pharmaceutical composition is a tablet.

33. A controlled-release pharmaceutical composition of claim 31, wherein the pharmaceutical composition is administered orally, parenterally, by inhalation spray, topically, rectally, nasally, buccally, vaginally or via an implanted reservoir.

34. A controlled-release pharmaceutical composition of claim 32, wherein the pharmaceutical composition is a tablet which, upon administration to a mammal, releases substantially all of the active ingredient in the mammal's small intestine.

35. A method of making microspheres comprising:

(a) dispersing a first pH insensitive hydrophobic polymer, a second pH-sensitive hydrophobic polymer, and an active ingredient in an organic solvent to form a polymer solution phase;

(b) emulsifying the polymer solution phase into a second continuous phase comprising a second solvent and a surfactant to form an emulsified dispersion system; and

(c) agitating the emulsified dispersion system and evaporating the organic solvent there from to form the microspheres

wherein (1) the concentration of the second polymer as a percentage of total polymer in the polymer solution phase ranges from around 0.25% to 10% and total polymer concentration in the polymer solution phase ranges from around 5% to around 35% (2) microsphere particle diameter ranges from approximately 25μm to approximately 1,000μm (3) the weight percentage of active ingredient in a microsphere ranges from around 5% to around 40%, and (4) active ingredient concentration is highest in the microsphere core.

36. The method of claim 35, wherein:

(a) the first and second polymers are selected from the group consisting of cross-linked polyvinyl alcohol, , polyvinyl chlorides, , regenerated insoluble non-erodible cellulose, acylated cellulose, esterified celluloses, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate diethyl-aminoacetate, polyurethanes, polycarbonates, and microporous polymers formed by co-precipitation of a polycation and a polyanion modified insoluble collagen;

(b) the organic solvent is an alcohol, acetonitrile, or ketone, or mixture thereof;

(c) the second solvent is silicone oil, sesame oil, soybean oil, corn oil, cottonseed oil, coconut oil, linseed oil, mineral oil, n-hexane, n-heptane, or mixtures thereof; and

(d) the surfactant is an anionic surfactant, nonionic surfactant, polyoxyethylene-castor oil derivative, polyvinylpyrrolidone, polyvinyl alcohol, carboxymethylcellulose, lecithin, gelatin, hyaluronic acid, or sorbitan sesquioleate, or mixtures thereof.

37. The method of claim 35, wherein the first and second polymers are selected from the group consisting of cellulose acetate dimethylamino acetate, cellulose acetate ethyl and methyl carbonate, cellulose acetate phthalate, cellulose acetate succinate, cellulose acetate chloroacetate, cellulose diacetate, cellulose triacetate, cellulose acetate ethyl oxalate, cellulose acetate methyl and butyl sulfonate, cellulose acetate octate, cellulose acetate laurate, cellulose acetate p-toluene sulfonate, cellulose acetate ethyl and methyl carbomate, cellulose acetate valerate, cellulose acetate maleate, and combinations and mixtures thereof.

38. The method of claim 35, wherein the first and second polymers are selected from the group consisting of cellulose acetate, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose propionate butyrate, and combinations and mixtures thereof.

39. The method of claim 35, wherein the first polymer is cellulose acetate butyrate (CAB) and the second polymer is cellulose acetate phthalate (CAP).

40. The method of claim 39, wherein the total concentration of polymer in the polymer solution phase is between around 5% to around 15%.

41. The method of claim 40, wherein the total concentration of CAP in the polymer solution phase as a percentage of total polymer is between around 1% to 3%.

42. The method of claim 41, wherein the average microsphere size is 100 μm to 700 μm.

43. The method of claim 42, wherein the total concentration of CAB in the polymer solution phase is between around 7% to around 9%, the total concentration of CAP in the polymer solution phase as a percentage of total polymer is between around 1% to 3%, and the microspheres are 150 μm to approximately 350 μm in size.

44. The method of claim 43, wherein the microspheres comprise up to around 35% by weight of one or more of the following active ingredients: an alpha-adrenergic agonist an analgesic or anti-migraine agent, an anti-allergic agent, an anesthetic agent, an anoretic agent, a anti-bacterial (antibiotic) agent an anti-cancer agent, an anti-cholinergic agents an anti-diabetic agent, an anti-emetic agent, an anti-fungal agent an antihistamine agent, an anti-hyperlipoproteinemic agent, an anti-hyperthyroid agent , an anti-inflammatory or corticoid agent, an anti-malarial agent, an anti-Parkinson's or Anti-Alzheimer's agent, an anti-psychotic, anti-anxiety or anti-depressant agent, an anti-ulcerative agent, an anti-viral agent, an anxiolytic agent, a B-Adrenergic agonist agent, a bronchodilator, a cardioactive agent, a central nervous system stimulant, a cholinergic agent, a muscle relaxant, and a narcotic antagonist agent.

45. The method of claim 43, wherein the organic solvent is acetone, sorbitan sesquioleate is used to emulsify the dispersion system, and the active ingredient is theophylline.

46. The method of claim 43, wherein the microspheres, upon dissolution in an aqueous environment having a pH of around 5 or 6 or greater, substantially all of the active ingredient is released from the microspheres in between around 12 to 24 hours.

47. The method of claim 43, wherein substantially all of the second polymer dissolves in the aqueous environment to release of substantially all of the active ingredient from the microspheres.

48. A method of making microspheres comprising:

(a) dispersing a first pH insensitive hydrophobic polymer, a second water-swellable polymer, and an active ingredient in an organic solvent to form a polymer solution phase;

(b) emulsifying the polymer solution phase into a second continuous phase comprising a second solvent and a surfactant to form an emulsified dispersion system; and

(c) agitating the emulsified dispersion system and evaporating the organic solvent there from to form the microspheres
wherein (1) the concentration of the second polymer as a percentage of total polymer in the polymer solution phase ranges from around 0.25% to 10%, total polymer concentration in the polymer solution phase ranges from around 5% to around 35%, and the viscosity of the polymer solution phase ranges from around 50 cps to around 1000 cps
(2) microsphere particle diameter ranges from approximately 25μm to approximately 1,000μm (3) the weight percentage of active ingredient in a microsphere ranges from around 5% to around 50%; and (4) active ingredient concentration is highest in the microsphere core.

49. The method of claim 48, wherein:

(a) the first polymer is selected from the group consisting of cross-linked polyvinyl alcohol, polyolefins, polyvinyl chlorides, acylated cellulose, esterified celluloses, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate diethyl-aminoacetate, polyurethanes, polycarbonates, and microporous polymers formed by co-precipitation of a polycation and a polyanion modified insoluble collagen;

(b) the second polymer is selected from the group consisting of a low-substituted cellulose ether or internally cross-linked cellulose derivatives of sodium carboxymethylcellulose, hydroxypropyl-methylcellulose (HPMC), a hydroxypropylcellulose (HPC), a poly(ethylene oxide), or a hydrogel forming polymer;

(c) the organic solvent is an alcohol, acetonitrile, or ketone, or mixture thereof;

(d) the second solvent is silicone oil, sesame oil, soybean oil, corn oil, cottonseed oil, coconut oil, linseed oil, mineral oil, n-hexane, n-heptane, or mixtures thereof; and

(e) the surfactant is an anionic surfactant, nonionic surfactant, polyoxyethylene-castor oil derivative, polyvinylpyrrolidone, polyvinyl alcohol, lecithin, or sorbitan sesquioleate, or mixtures thereof.

50. The method of claim 48, wherein the first polymer is selected from the group consisting of cellulose acetate dimethylamino acetate, cellulose acetate ethyl and methyl carbonate, cellulose acetate succinate, cellulose acetate chloroacetate, cellulose diacetate, cellulose triacetate, cellulose acetate ethyl oxalate, cellulose acetate methyl and butyl sulfonate, cellulose acetate octate, cellulose acetate laurate, cellulose acetate p-toluene sulfonate, cellulose acetate ethyl and methyl carbamate, cellulose acetate valerate, cellulose acetate maleate, and combinations and mixtures thereof.

51. The method of claim 48, wherein the first polymer is selected from the group consisting of cellulose acetate, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose propionate butyrate, and combinations and mixtures thereof.

52. The method of claim 48, wherein the second polymer is a hydrogel forming polymer.

53. The method of claim 48, wherein the first polymer is cellulose acetate butyrate (CAB) and the second polymer is hydroxypropylcellulose (HPC).

54. The method of claim 53, wherein the total concentration of polymer in the polymer solution phase is between around 5% to around 35%.

55. The method of claim 54, wherein the total concentration of HPC in the polymer solution phase as a percentage of total polymer is between around 0.25% to 10%.

56. The method of claim 55, wherein the average microsphere size is 100 μm to 400 μm.

57. The method of claim 55, wherein the total concentration of CAB in the polymer solution phase is between around 7% to around 9%, the total concentration of HPC in the polymer solution phase as a percentage of total polymer is between around 0.5% to 3%, and the microspheres are 150 μm to approximately 350 μm in size.

58. The method of claim 55, wherein the microspheres comprise up to around 35% by weight of one or more of the following active ingredients: an alpha-adrenergic agonist an analgesic or anti-migraine agent, an anti-allergic agent, an anesthetic agent, an anoretic agent, a anti-bacterial (antibiotic) agent an anti-cancer agent, an anti-cholinergic agents an anti-diabetic agent, an anti-emetic agent, an anti-fungal agent an antihistamine agent, an anti-hyperlipoproteinemic agent, an anti-hyperthyroid agent , an anti-inflammatory or corticoid agent, an anti-malarial agent, an anti-Parkinson's or Anti-Alzheimer's agent, an anti-psychotic, anti-anxiety or anti-depressant agent, an anti-ulcerative agent, an anti-viral agent, an anxiolytic agent, a B-Adrenergic agonist agent, a bronchodilator, a cardioactive agent, a central nervous system stimulant, a cholinergic agent, a muscle relaxant, and a narcotic antagonist agent.

59. The method of claim 55, wherein the organic solvent is acetone, Arlacel 83 is used to emulsify the dispersion system, and the active ingredient is theophylline.

60. The method of claim 55, wherein, upon dissolution in an aqueous environment having a pH of around 5 or 6 or greater, substantially all of the active ingredient is released from the microspheres in between around 12 to 24 hours.